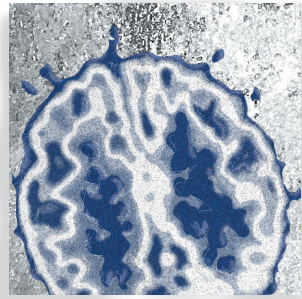# Translational research

A systematic review of the neural bases of psychotherapy for anxiety and related disorders

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Brain imaging studies over two decades have delineated the neural circuitry of anxiety and related disorders, particularly regions involved in fear processing and in obsessive-compulsive symptoms. The neural circuitry of fear processing involves the amygdala, anterior cingulate and insular cortex, while cortico-striatal-thalamic circuitry plays a key role in obsessive-compulsive disorder. More recently, neuroimaging studies have examined how psychotherapy for anxiety and related disorders impacts on these neural circuits. Here we conduct a systematic review of the findings of such work, which yielded 19 functional magnetic resonance imaging studies examining the neural bases of cognitive-behavioral therapy (CBT) in 509 patients with anxiety and related disorders. We conclude that, although each of these related disorders is mediated by somewhat different neural circuitry, CBT may act in a similar way to increase prefrontal control of subcortical structures. These findings are consistent with an emphasis in cognitive-affective neuroscience on the potential therapeutic value of enhancing emotional regulation in various psychiatric conditions.

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Introduction

Basic and clinical studies have led to advances in our understanding of the neural circuitry of anxiety and related disorders. Animal studies, for example, have highlighted the role of the amygdala in fear conditioning[1] and of the striatum in mediating grooming behaviors.[2] Structural and functional brain imaging studies in patients with anxiety and related disorders have shown alterations in analogous regions, identifying a "fear network" incorporating the amygdala, anterior cingulate, and insular cortex,[3] and emphasizing the role of cortico-striatal-thalamic-cortical circuitry in obsessive-compulsive and related disorders.[4] The cognitive-affective neuroscience of anxiety and related disorders points to the role of discrete types of "false alarm" that can be targeted effectively with psychotherapy.[5] More recently, a number of functional magnetic resonance imaging (fMRI) studies have begun to explore the impact of psychotherapy on these neural circuits. Here we review this literature, exploring the question of how cognitive-

behavioral therapy (CBT) in particular alters neural circuitry in anxiety and related disorders, after considering animal and human models of anxiety and related disorders.

Animal models of anxiety and related disorders

Animal models have provided valuable insights into the neural circuitry of key cognitive-affective processes relevant to anxiety and related disorders. Basic research on the neurobiology of fear conditioning, for example, has contributed to our understanding of the neural circuitry of the anxiety disorders and of trauma- and stressor-related disorders such as post-traumatic stress disorder (PTSD). Work on the neurobiology of social dominance and submission has arguably been particularly relevant to understanding the neural circuitry of social anxiety disorder (SAD). Animal models of repetitive grooming or other stereotypic behaviors may be useful in providing insights into the neuroanatomy of obsessive-compulsive disorder (OCD). Here we briefly review this work.

The neural circuitry of fear conditioning and fear extinction is particularly well conserved across mammalian species. Animal studies of the neural circuitry of fear conditioning have established that stimulation of the amygdala produces physiological and behavioral responses akin to anxiety and panic.[6,7] Stimulation of the periaqueductal gray, a brain stem nucleus, also evokes fear responses, including fast muscle contractions, twitching, and blinking.[8,9] Moreover, acute stress may diminish the effective regulation of fear, presumably by altering synaptic excitation of glutamate receptors in the prefrontal cortex, as seen in rodent stress.[10] Additionally, the role of hippocampal function in contextual fear learning—or Pavlovian conditioning—is well-documented.[11] In terms of fear reconsolidation and extinction, medial prefrontal cortex and connections between the amygdala, hippocampus, and entorhinal cortex play a key role.[12]

Social dominance models have been studied in subordinate primates,[13] and implicate mesolimbic regions such as the amygdala, hippocampus, and striatum in the neuropathology of SAD and anxiety disorders. For example, shrinkage of hippocampal volumes can occur in mice exposed to social stress,[14] with one hypothesis being that this is mediated by hypothalamic–pituitary–adrenal (HPA) axis cortisol release.[15] Further, hyperactivation of the HPA axis and impaired neurotransmission in the striatum is associated with lower social status and submissiveness in primates.[15,16] Conversely, gray matter volume enlargement in the amygdala, hippocampus, striatum, hypothalamus, and raphe nucleus of the brain stem is observed in Macaque monkeys with higher social status.[17] Thus, social fear conditioning and stress subordination/social submissiveness appear to involve volume reduction and hyperstimulation of the mesolimbic pathway.[13]

A range of animal studies have examined the neuroanatomy of grooming and other stereotypies that are relevant to OCD.[18] Such stereotypies range from simple motor perseveration to more complex behaviors[19] and there is a growing understanding of the underlying neuroanatomy. In an early study, persistent, stereotyped movements in the aftermath of social deprivation in nonhuman primates were associated with alterations in the cytoarchitecture of the striatum.[20] More recent work in mice has found that the dorsal medial striatum and orbitofrontal cortex (OFC) are more engaged, whereas the dorsal lateral striatum appears less engaged when mice lever-press with a goal-directed versus habitual action strategy respectively.[21] More recently, optogenetics methods have been used to manipulate neural transmission in rodents, and have demonstrated that chronic hyperstimulation of an excitatory circuit between glutamatergic neurons in the orbitofrontal cortex and the ventromedial striatum triggers compulsive behavior.[19,22]

Neurocircuitry of anxiety and related disorders

While animal models provide important insights, brain imaging studies using fMRI link uniquely human cognitions and behaviors to the neuropathology of anxiety and related disorders. Functional brain imaging studies typically examine responses to specific anxiety-provoking stimuli, such as angry faces or disturbing scenes, or during cognitive tasks such as response inhibition. These paradigms have highlighted common patterns of neural activation in those with anxiety and related disorders and have led to the development of neural circuitry models. For example, the neural substrates of conditioned fear have emphasized the role of amygdala hypersensitivity; the lateral amygdala for fear acquisition and the central nucleus for fear behaviors.[1,23]

Furthermore, in OCD hyperactivation of the cortico-striatal-thalamic-cortical (CSTC) network, specifically involving the lateral and medial OFC and the dorsal anterior cingulate cortex circuitry, is exacerbated during anxiety-provoking visual stimulus presentation and underlies deficits in fear extinction and behavioral inhibition.[24] Hippocampal function mediates appreciation of safe contexts and explicit learning/memory, and deficits in fear extinction and contextual learning in those with anxiety disorders coincide with reduced hippocampal activation to anxiety-provoking stimuli.[25]

Along with the amygdala and the CTSC networks, activation of the insular cortex, a brain region associated with perceptions of bodily sensations (interoceptive awareness) and emotion regulation also seems to be involved in the experience of anxiety, disgust, and obsessive-compulsive symptoms.[26,3,27] For example, altered interoceptive awareness, or an inability to effectively process bodily sensation, is prominent in anxiety states, and could be due to an augmented detection of the difference between observed and expected bodily states.[28] Further, insula function contributes to the interface between basic interoception and self-referential belief states that are driven by prefrontal cortex processes.[29] However, insula involvement in heightened anxiety is suggested to be due, not to faulty interoceptive processing per se, but to an amplified self-referential and discrepant prediction about bodily state[29] that may originate in prefrontal cortex and be associated with dysregulated top-down emotion regulation.[30,31]

While fMRI studies often utilize symptom-provocation paradigms with disorder-specific stimuli, or cognitive tasks, resting-state studies, on the other hand, measure neural activation at rest and further contribute to our understanding of the neural circuitry of anxiety and related disorders.[32] For example, a recent meta-analysis examining 28 resting state studies in patients with anxiety disorders demonstrated similarities across PTSD, PD, GAD, SAD, and OCD in broad connectivity alterations between limbic regions—namely, the bilateral amygdalae, insula, and regions associated with the default mode network (DMN—for self-referential thought), central executive network (CEN—for control of emotion) and salience network (SN—for arousal).[33] However, resting state connectivity in specific anxiety disorders may be highly variable, and to date only OCD demonstrates consistent functional alterations in the corticostriatal circuitry and the DMN.[33]

While prefrontal cortex and limbic connectivity is broadly implicated in dysregulation of emotional processing in anxiety disorders in general, discrete functional differences are observed in specific anxiety disorders, and these will now be considered.

PTSD

PTSD is a trauma- and stressor-related disorder that affects individuals who have been exposed to a substantial traumatic event (eg, combat, interpersonal violence, natural disaster), and is characterized by intrusive memories of the trauma, avoidance of related cues, and hyperarousal.[34] Functional imaging studies over the past two decades have demonstrated that PTSD is accompanied by heightened activation of the amygdala, particularly the lateral and basal amygdala, with aberrant activation between the amygdala and medial prefrontal cortex, hippocampus, and insula.[35]Specifically, excessive activation of the amygdala in those with PTSD is consistently shown by fMRI studies in response to trauma-arousing words.[25,36-38] It is suggested by a number of fMRI studies that amygdala hyperactivation is due to ineffective inhibitory control by the medial prefrontal cortex,[38] and a recent review confirmed that for PTSD, as opposed to other anxiety disorders, activation of the anterior cingulate cortex (ACC), which forms part of the mPFC inhibitory network, is consistently reduced.[3] Additionally, a large meta-analysis of 846 PTSD patients found reduced bilateral hippocampal volume, particularly on the left side.[39] The No/Go task, a paradigm where participants are required to withhold their button press response when a stop stimulus is presented, has been used in fMRI studies to demonstrate deficits in response inhibition, and is associated with reduced medial PFC and ACC activation in those with PTSD.[40,41] Additionally, hippocampal structure and functional connectivity with PFC is reported to be reduced in those with PTSD, which could contribute to deficits in fear conditioning, fear extinction, and may reflect neurotoxicity associated with significant trauma.[42,43.]

PD

PD is characterized by panic attacks and hyperarousal[34] and involves neural dysfunction in the fear network, again involving amygdala hypersensitivity, and dysfunctional emotion regulation in the PFC.[44] An early

neuroanatomical hypothesis of PD proposed that brain stem and hypothalamus were responsible for the stress and panic responses; the mesolimbic pathway (eg, the amygdala and hippocampus) for fear anticipation, and the prefrontal cortex for phobic reactions and emotion dysregulation.[45] More recently this hypothesis has been refined to emphasise "crosstalk" and functional connectivity patterns prevalent in PD, between corticolimbic areas, namely the OFC and ACC for emotion regulation, and the amygdala, hippocampus, and insula for hyperarousal.[46] fMRI studies to date support a model of PD that emphasizes cognitive impairment in fear processing[46] in that excessive contextual fear learning is processed by the hippocampus, exacerbating amygdala hypersensitivity to threat cues and ineffective emotion regulation via the PFC, which together results in exaggerated pathological fear.

GAD

GAD is characterized by debilitating, chronic, excessive, and uncontrollable worry about a variety of topics.[34] In contrast to the other anxiety disorders, fMRI studies of GAD have reported hypofunction of prefrontal and anterior cingulate regions, as documented in a recent review.[47] The review included 14 fMRI studies and examined the neural correlates of the contemporary models of GAD, namely: 10 studies adhering to the emotional dysregulation theory.[48] The other studies included in the review examined other related models, namely; the conditioned fear overgeneralization model and the intolerance of uncertainty theory.[47] The emotion dysregulation theory asserts that patients with GAD experience emotional hyperarousal,[49] contributing to maladaptive emotion regulation and unsuccessful attempts to either minimize or over-control emotions. Emotional dysregulation in GAD across 10 fMRI studies to date has been linked to a reduced PFC and ACC activation during emotion regulation tasks (for review, see refs 47,49).

SAD

SAD is defined as an excessive fear of social situations; such that avoidance or significant distress ensues to disrupt normal functioning.[34] Functional neuroimaging studies of SAD have found increased limbic activation especially in the amygdala and particularly in response to emotional stimuli of a social and self-critical nature.[50]

Additionally, dysfunctional interplay between the limbic system and prefrontal cortex regions in SAD (eg, medial prefrontal cortex, dorsal raphe, striatum, locus coeruleus, insular cortex, and anterior cingulate cortex), involving γ-aminobutyric acid (GABA), dopaminergic, and oxytocin neurotransmitter systems may underlie symptoms and volumetric changes.[50-52] In a recent meta-analysis of brain function in 17 studies of SAD patients, increased limbic processing in response to emotional faces was significant, specifically hyperactivation of the amygdala, the parahippocampal gyrus, and the globus pallidus in comparison with healthy controls.[53] Additionally, hyperactivation of the insula, putamen, the superior temporal gyrus, medial frontal regions and the cuneus was observed in the SAD cases compared with Williams-Beuren Syndrome—a disorder on the opposite end of the social anxiety spectrum.[53] Thus, increased limbic activation to socially emotive stimuli appears to be present in those with SAD, and it is possible that, consistent with other anxiety disorders, inefficient top-down regulation by prefrontal cortex networks of excessive limbic responses may contribute to social anxiety symptoms.

OCD

OCD is characterized by recurring thoughts and beliefs (obsessions), as well as physical or mental acts performed repeatedly that are difficult to resist (compulsions).[34] Detailed modeling of the neural circuitry of OCD has emerged from various imaging studies. Early work[54] proposed that the behaviorally disinhibiting direct basal ganglia pathway and the behaviorally inhibiting or moderating indirect basal ganglia system alters "neural tone" and may mediate the expression of OCD symptoms. More recent studies of the neuroanatomy and function of OCD have continued to implicate CSTC circuits in the pathophysiology of OCD.[19] The CSTC circuitry is comprised of parallel loops, which appear to support inhibitory (eg, freezing, motor repetition) or excitatory (eg, compulsivity, fear conditioning) behaviors and cognitions, and interplay between different areas of these loops may explain the different OCD symptom dimensions (eg, hoarding, checking, cleaning, counting).[55] Such models are supported by a recent multicenter mega-analysis,[56] which found reduction in ACC, dorsomedial prefrontal cortex, and inferior frontal gyrus volumes in OCD, with group-by-age interactions in striatum, OFC, and insula. In line with

functional deficits in prefrontal cortex circuitry in those with OCD, a recent meta-analysis of structural differences reported reduction in prefrontal cortex volumes, but also increased striatal volumes.[4] Aberrant activation CSTC circuitry may also explain executive dysfunction seen in OCD.[57] For example, a recent meta-analysis of 110 previous studies revealed that individuals with OCD are impaired on tasks measuring most aspects of executive function and that these impairments are not influenced by motor slowness or depression.[58] Executive dysfunction may be associated with excessive modulatory top-down prefrontal cortical activation of excessive basal ganglia network activation.[59]

A systematic review of the neural correlates of CBT for anxiety and related disorders

Animal models and functional brain imaging studies provide an important foundation for the investigation of how CBT alters the neurocircuitry of anxiety and related disorders. CBT remains the most widely recommended first-line psychotherapy for anxiety and related disorders[60] and aims to alter affect, behavior, and cognitions (A-B-C) that contribute to misperceptions of threat and behavior, and to strengthen self-awareness of emotional responses to anxiety-related stimuli. A key outcome of CBT is better emotion regulation of anxiety responses.[61] From this perspective, we now systematically review functional MRI studies that have examined the neural correlates of CBT for each of the main anxiety and related disorders in turn. The neural correlates of anxiety disorders are summarized in *Figure 1*.

Literature search

We searched PubMed, Medline, and Google Scholar, and conducted a manual search of the publication reference lists from 1995 until May 2015 using the following search criteria: FMRI + CBT + ANXIETY; FMRI + CBT + POST TRAUMATIC STRESS DISORDER; FMRI + CBT + PANIC DISORDER; FMRI + CBT + GENERALISED ANXIETY DISORDER: FMRI + CBT + SOCIAL ANXIETY DISORDER; FMRI + CBT + OBSESSIVE COMPULSIVE DISORDER. We also substituted FMRI for MRI and NEURAL, and CBT for PSYCHOTHERAPY as additional searches. Publications were included if they were: (i) written in English; (ii) used CBT and not other methods (eg, other

psychological therapies or pharmacotherapy); (iii) used fMRI and not other imaging modalities (which are outside the scope of the aims of this article); (iv) examined patient populations other than anxiety and related disorders. This systematic search yielded 19 fMRI studies for inclusion in this review. We now describe the findings in relation to the separate anxiety and related disorders. See *Table I* for details of included studies. Additional details regarding these studies will be found in the online version of this *Table*.

PTSD

Two fMRI studies have identified neural correlates of CBT for PTSD, which has the neural characteristics of hyperactivation of the amygdala and reduced PFC and ACC activation. In the first fMRI study, 14 PTSD patients' neural responses to masked fearful faces were measured before and after 8 weeks of CBT that involved education, imagined and in vivo exposure, and cognitive therapy.[62] The authors found that 7 patients only were treatment responders (eg, at least 50% improvement on symptom scores), and that poor treatment response was associated with pretreatment increases in bilateral amygdala and ventral ACC. The authors suggest that excessive pretreatment neural responses in these regions may signal deficits in emotion regulation during treatment and may hinder CBT efficacy. A second fMRI study used the No/Go task to examine inhibitory neural function following 8 weeks' CBT treatment.[63] It was found that after CBT there was greater left dorsal striatal and frontal network activation during inhibitory control, which was associated with lower PTSD symptom severity, indicating that improvements to inhibitory control contribute to better treatment response.

PD

Four fMRI studies to date have examined the neural correlates of CBT for PD. PD is associated with amygdala hypersensitivity and dysregulation in the PFC and CBT has been shown to effectively alter these neural patterns. The first study compared 42 PD patients with healthy controls and found that a 12-week course of manualized CBT altered neural responses to fear-conditioned stimuli.[64] Specifically, reduced left inferior frontal gyrus (IFG) was observed post-CBT treatment in the PD group, as well as increased functional connectivity between the

IFG and regions of the fear network, namely the amygdalae, insulae, and anterior cingulate cortex. In another study, 49 medication-free PD patients, who received manualized CBT treatment and who were categorized as either responders or nonresponders based on at least 50% symptom reduction, were measured for neural responses during fear conditioning.[65] The authors reported that successful treatment was associated with an increase in right hippocampal activation when using cognitive strategies in response to fear-based stimuli. Furthermore, significant symptom reduction was associated with an inhibitory functional coupling between the anterior cingulate cortex and the amygdala that did not change over time. The authors suggest that neuroplasticity within frontal-amygdala networks may mediate improvements in safety signaling. In another study, CBT treatment efficacy in 23 PD patients was best predicted, during maintenance of emotion by activation in the insula/anterior cingulate cortex, and during reappraisal of emotion by

activation in the occipital and supramarginal gyrus.[66] In the largest multicenter study of the effects of CBT on neural correlates of symptom reduction in patients with PD,[67] 49 patients who completed at least 4 weeks of CBT treatment were examined using a fear conditioning task. The authors reported that neural activation to fear conditioning and extinction predicted whether patients became responders or nonresponders after treatment, with 70% accuracy. Fear conditioning was associated with increased neural responses in the precentral gyrus, occipital cortex, and OFC. Fear extinction by contrast was associated with increased activation in the putamen, paracingulate cortex, and occipital and frontal cortices.

GAD

Four studies have examined the effects of CBT on neural activation in patients with GAD, which is characterized by hypoactivation in the mPFC and ACC, per-
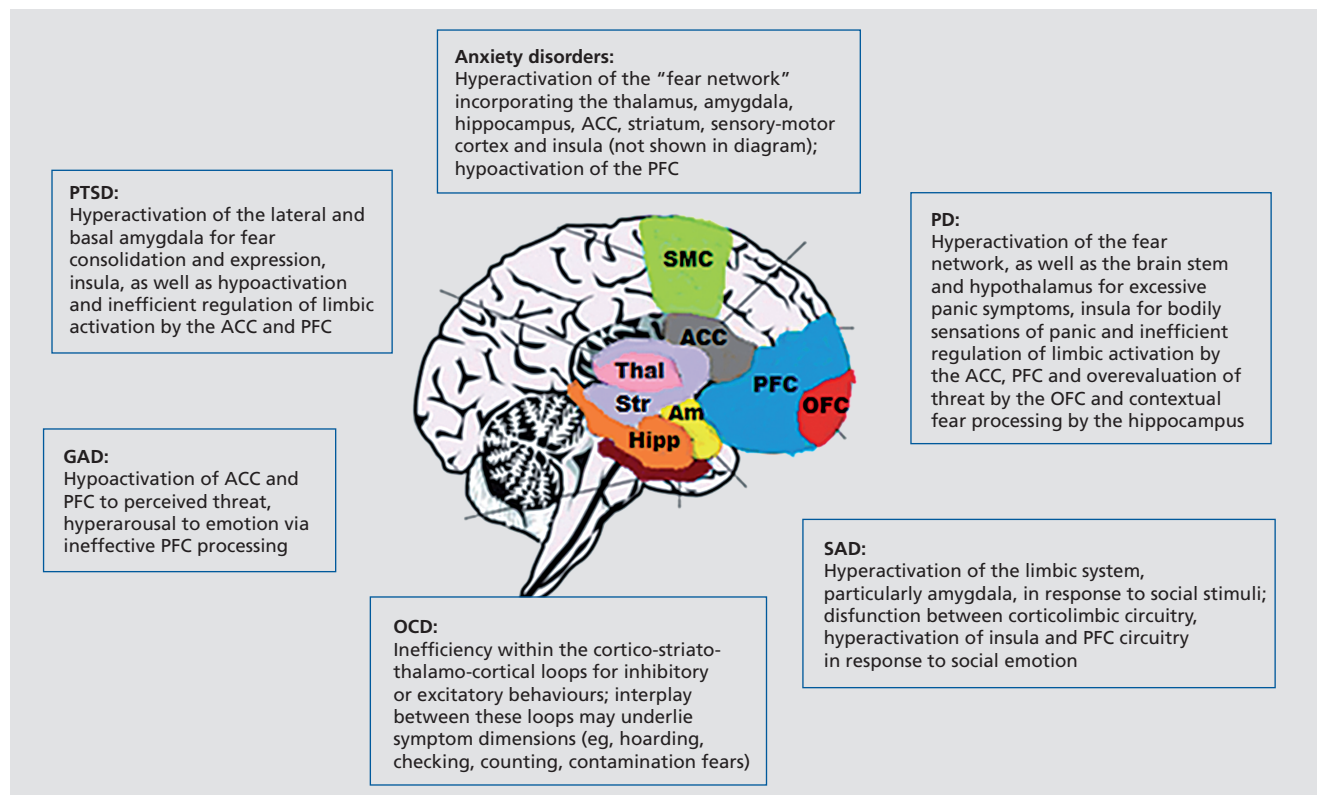
Figure 1. A schematic diagram summarizing the neural correlates of anxiety and related disorders. PTSD, post-traumatic stress disorder; PD, panic disorder; GAD, generalized anxiety disorder; SAD, social anxiety disorder; OCD, obsessive-compulsive disorder; SMC, sensory-motor cortex; ACC, anterior cingulate cortex; PFC, prefrontal cortex; OFC, orbitofrontal cortex; Thal, thalamus; Str, striatum; Am, amygdala; Hipp, hippocampus

haps due to excessive limbic responsivity to perceived threat stimuli. In the first fMRI study with a facial emotion recognition task, 7 pediatric patients with a predominant GAD diagnosis were examined after an 8-week course of CBT that focused on exposure and skills training (versus 7 patients who chose SSRI treatment).[68] It was found that left amygdala hyperactivation prior to treatment predicted a reduction in clinical severity scores following CBT. In a similar fMRI study using an emotional probe task, 7 adolescents with GAD showed increased right vlPFC response following 8 weeks of CBT treatment.[69] The authors conclude that increased vlPFC response is likely indicative of improvements to modulation of anxiety responses originating in the amygdala. In a third study of 25 adults being treated with CBT for GAD, hippocampal activation during maintenance of response to emotional stimuli, and anterior insula, superior temporal, supramarginal, and superior frontal gyrus activation during reappraisal of emotion were among the best predictors of better treatment response.[66] In the final study to date, of 21 adults with GAD who undertook CBT treatment compared with healthy controls, at pretreatment those with GAD showed reduced responses in the amygdala, insula, and anterior cingulate to pictures of happy faces, and greater amygdala-insula connectivity.[70] After 10 sessions of CBT there was attenuated amygdalar and subgenual anterior cingulate activation to fear/angry faces and heightened insular responses to happy faces with no effects on connectivity. The authors suggest a dual process effect of CBT on those with GAD, in that neural responses to positive stimuli are heightened and neural responses to fearful stimuli attenuated. This may perhaps be due to strengthened PFC functioning that is better able to regulate the experience of positive and negative emotions.

SAD

The neural correlates of SAD are an excessive limbic response to socially emotive stimuli. Four studies have so far examined the effects of CBT on patients with SAD. The first study examined neural responses to emotional faces/scenes in 39 patients with SAD being treated with CBT.[71] The authors report increased neural activation in temporal occipital regions to emotional stimuli before treatment predicts lower clinical severity after CBT. Similarly, in a study examining the neural correlates of

a 12-week program of CBT in 14 patients with SAD, successful intervention predicts enhanced pretreatment activation to threatening faces in superior and middle temporal gyrus (for visual processing) and dorsal anterior cingulate cortex, dorsomedial prefrontal cortex (for cognitive regulation of emotion).[72] Furthermore, this study revealed that greater threat processing of fearful faces prior to treatment corresponds with greater prefrontal cortex and insula activation in the SAD group. Another study examined the effects of cognitive reappraisal after 16 individual sessions of CBT in 75 patients with SAD.[73] More positive responses and reappraisals of negative self-belief statements at the end of treatment were associated with greater prefrontal cortex activation and greater connectivity between prefrontal cortex and amygdala that coincided with reductions in negative emotion ratings. A similar later study by the same group, this time examining the neural correlates of emotional responsivity to social evaluation after the same type of CBT was conducted in a subset of 59 patients with SAD.[74] CBT altered emotional reactivity in terms of increased right superior frontal gyrus (SFG), inferior parietal lobule (IPL) and middle occipital gyrus (MOG) activation during social praise. In contrast, CBT was followed by increases in right SFG and IPL and decreases in left posterior superior temporal gyrus (pSTG) during social criticism. Finally, CBT increased brain responses in right SFG and MOG, and decreased left pSTG activation during reappraisal of emotion.

OCD

The neural correlates of OCD involve cortico-striato-thalamo-cortical (CSTC) networks, for example, excessive PFC modulation of excessive limbic responsivity to emotional stimuli, although the various symptom dimensions of OCD likely reflect different neural patterns within the CSTC loops. Five fMRI studies so far have examined the effects of CBT in pediatric and adult samples. The first fMRI study used the Stroop task that evokes conflicting responses to stimulus targets that included symptom provocation in 10 outpatients with OCD.[75] The authors reported that after 12 weeks' of CBT there was a reduction in PFC activation to conflicting responses, and an increase in the parietal cortex and cerebellum to anxiety-provoking stimuli. A later reverse-learning (RL) fMRI study measured the effects of CBT using exposure and response prevention on frontostriatal circuitry in 10

patients with OCD.[76] It was found that before CBT, RL was associated with reduced OFC and striatal activation (caudate), and that after CBT there was increased striatal activation (putamen) during RL. A later fMRI study used the Flanker task to probe conflict processing in a pediatric sample of 25 with OCD who completed 8 weeks of CBT.[77] The authors concluded that the OCD group had increased ACC and bilateral insula activation during er-

ror/high conflict tasks that was only partially altered by CBT. In a more recent fMRI study examining the effects of 3 months' CBT on neural function during a personalized image exposure probe task in 35 OCD patients, anterior cingulate and orbitofrontal cortex activation was higher during exposure to personalized obsession-inducing images.[78] Further, activation to the anxiety-provoking images, in the anterior cingulate and left orbitofrontal

Study (year)	Title of paper	Participant characteristics	CBT intervention	Brain imaging paradigm	Summary of findings (from publication abstracts)
PTSD (n=2)					
Bryant et al, 2008	Amygdala and ventral anterior cingulate activation predicts treatment response to cognitive behaviour therapy for post-traumatic stress disorder	14 adults; 6 were taking SSRI medication; 8 females, 6 males, mean age=42.2 years; 9 had comorbid major depressive disorder; 1 had comorbid panic disorder; assault, motor accident, police incident or hold up	Eight sessions of CBT that comprised education, imaginal and in vivo exposure, and cognitive therapy/cognitive restructuring. Treatment response was assessed 6 months after therapy completion[80]	Neural response to fearful and neutral facial expressions presented rapidly in a backwards masking paradigm	Seven patients were treatment responders (defined as a reduction of 50% of pre-treatment scores) and seven were nonresponders. Poor improvement after treatment was associated with greater bilateral amygdala and ventral anterior cingulate activation in response to masked fearful faces.
Falconer et al, 2013	Inhibitory neural activity predicts response to cognitive-behavioral therapy for post-traumatic stress disorder	13 adults; 6 were taking SSRI medication 8 females, 5 males; mean age=38.3 years; 8 had comorbid major depressive disorder, 1 had comorbid panic disorder, physical assault or motor accident	Eight once-weekly sessions of CBT. PTSD severity was measured before treatment and again at 6 months following treatment completion	Go/No-Go task to examine neural correlates of inhibitory function	Greater activity in left dorsal striatal and frontal networks during inhibitory control was associated with lower PTSD symptom severity after treatment.
PD (n=4)					
Kircher et al, 2013	Effect of cognitive-behavioral therapy on neural correlates of fear conditioning in panic disorder	42 medication free adults; 29 females,13 males; mean age=35.4 years; 31 participants had comorbidity with major depressive disorder	12 twice-weekly sessions of manualized CBT, including education and exposure techniques (RCT multicenter)[81]	Fear conditioning task	After CBT, reduced activation for the conditioned response in the left inferior frontal gyrus (IFG) and was correlated with reduction in agoraphobic symptoms after CBT. Patients compared to controls also demonstrated increased connectivity between the IFG and regions of the «fear network» (amygdalae, insulae, anterior cingulate cortex) across time.

Table I. FMRI studies of the neural correlates of cognitive behavioral therapy (CBT) in anxiety and related disorders. RCT, randomized controlled trial; PTSD, post-traumatic stress disorder; GAD, generalized anxiaety disorder; OFC, orbitofrontal cortex; VLPFC, ventrolateral prefrontal cortex

Study (year)	Title of paper	Participant characteristics	CBT intervention	Brain imaging paradigm	Summary of findings (from publication abstracts)
Lueken et al, 2013	Neural substrates of treatment response to cognitive-behavioral therapy in panic disorder with agoraphobia	49 medication free adults; 33 females, 16 males; mean age=35.3 years; comorbidity for unipolar depression and other anxiety disorders	Manualized treatment protocol consisted of 12 twice-weekly sessions with behavioral exposure in situ. Patients were randomly assigned to one of two CBT arms, which differed only with regard to therapist-guided or nonguided exposure sessions (six out of 12 sessions)[82]	Fear conditioning and extinction task	At baseline, nonresponders exhibited enhanced activation in the right pregenual anterior cingulate cortex, the hippocampus, and the amygdala in response to a safety signal. While this activation pattern partly resolved in nonresponders after CBT, successful treatment was characterized by increased right hippocampal activation when processing stimulus contingencies. Treatment response was associated with an inhibitory functional coupling between the anterior cingulate cortex and the amygdala that did not change over time
Ball et al, 2014	Single-subject anxiety treatment outcome prediction using functional neuroimaging.	48 medication free adults; 39 females, 9 males; mean age=31.7 years; comorbid for GAD	10 sessions of open-label weekly individual CBT[83]	Reduced (via cognitive reappraisal) or maintained their emotional responses to negative images	Activations in the hippocampus during maintenance and anterior insula, superior temporal, supramarginal, and superior frontal gyri during reappraisal were among the best predictors, with greater activation in responders than nonresponders.
Hahn et al, 2015	Predicting treatment response to cognitive behavioral therapy in panic disorder with agoraphobia by integrating local neural information	49 medication free adults; 33 females; 16 makes; mean age=35.3 years; comorbidity for unipolar depression and other anxiety disorders	Manualized treatment; 12 sessions of CBT 2 times a week focusing on behavioral exposure in situ. In the therapist-guided condition, the therapist accompanied the patient during exposure, whereas patients were instructed by the therapist but performed the exposure on their own in the nonguided condition[82]	Differential fear-conditioning task	Neural activation to fear conditioning and extinction predicted whether patients became responders or nonresponders after treatment, with 70% accuracy. Fear conditioning was associated with increased neural responses in the precentral gyrus, occipital cortex and OFC. Fear extinction by contrast was associated with increased activation in the putamen, paracingulate cortex, occipital and frontal cortices
GAD (n=4)					
McClure et al, 2007	fMRI predictors of treatment outcome in pediatric anxiety disorders.	15 medication free children/adolescents; 7 females, 8 males; mean age=11.7 years; 3 had comorbidity for social phobia;	8 weekly CBT for 60–90 min per session, focusing on manualized exposure and skills training based on the Social Effectiveness Therapy for Children (SET-C)[84,85]	Face-attention paradigm (afraid, happy, neutral, angry)	Negative associations between left amygdala activation and measures of post-treatment symptom improvement in the group

Table I. Continued

Study (year)	Title of paper	Participant characteristics	CBT intervention	Brain imaging paradigm	Summary of findings (from publication abstracts)
Maslowsky et al, 2010	A preliminary investigation of neural correlates of treatment in adolescents with generalized anxiety disorder.	7 medication free adults; 4 females, 3 males; mean age=13.4 years; comorbidity with social phobia, separation anxiety, attention deficit hyperactivity disorder; major depressive disorder	8 weekly CBT for 60–90 min per session, focusing on manualized exposure and skills training based on the Social Effectiveness Therapy for Children (SET-C)[84,85]	A probe detection task with emotional (angry, happy) and neutral faces allowed for assessment of neural response to threat	Increased right VLPFC activation after CBT
Ball et al, 2014	Single-subject anxiety treatment outcome prediction using functional neuroimaging.	48 medication free adults; 39 females, 9 males; mean age=31.7 years; comorbid for panic disorder	10 sessions of open-label weekly individual CBT[83]	Reduced (via cognitive reappraisal) or maintained their emotional responses to negative images	Activations in the hippocampus during maintenance and anterior insula, superior temporal, supramarginal, and superior frontal gyri during reappraisal were among the best predictors, with greater activation in responders than nonresponders.
Fonzo et al, 2014	Cognitive-behavioral therapy for generalized anxiety disorder is associated with attenuation of limbic activation to threat-related facial emotions.	21 medication free adults; 16 female, 5 male; mean age=34.3 years; comorbid for social anxiety disorder, obsessive-compulsive disorder, panic disorder, major depressive disorder	CBT Treatment was adapted from a computer-assisted primary care intervention for anxiety disorders (Craske et al 2011) and included psychoeducation, self-monitoring, breathing retraining, fear hierarchy, and relapse prevention) and three that were tailored specifically to the treatment of GAD (cognitive restructuring, imaginal exposure, and in-vivo exposure)	Facial emotion processing task (angry, happy, fear)	Reduced responses at pretreatment in the amygdala, insula, and anterior cingulate to happy faces, and greater amygdalo–insular connectivity. CBT was associated with attenuated amygdalar and subgenual anterior cingulate activation to fear/angry faces and heightened insular responses to the happy face comparison condition, but had no apparent effects on connectivity
SAD (n=4)					
Doehrmann et al, 2013	Predicting treatment response in social anxiety disorder from functional magnetic resonance imaging.	39 medication free adults (no other patient details given)	Group-based CBT (No other details given)	Brain responses to angry vs. neutral faces or emotional vs neutral scenes	Pretreatment brain responses for angry vs neutral faces in 2 occipitotemporal brain regions were significantly and positively associated with CBT outcome.
Klumpp et al, 2013	Neural predictors and mechanisms of cognitive behavioral therapy on threat processing in social anxiety disorder	14 medication free adults; 9 female, 5 male; mean age=28.07 years; no comorbidities	12 weeks of manualized individual CBT, which consisted of one 60-minute session per week[86]	Social signals of threat (fearful/angry faces) against positive signals (happy faces)	CBT-related brain changes involved a reduction in activity in insula, prefrontal, and extrastriate regions.

Table I. Continued

Study (year)	Title of paper	Participant characteristics	CBT intervention	Brain imaging paradigm	Summary of findings (from publication abstracts)
Goldin et al, 2013	Impact of cognitive behavioral therapy for social anxiety disorder on the neural dynamics of cognitive reappraisal of negative self-beliefs: randomized clinical trial	31 medication free adults (No other patient details given)	I-CBT was delivered using Managing Social Anxiety: A Cognitive-Behavioral Therapy Approach, a manualized treatment protocol which consisted of 16 individual one-hour sessions (except for the first in-session exposure session which lasted 1.5 hours) administered over 4 months. I-CBT covered: psychoeducation and orientation to CBT; cognitive restructuring skills; graduated exposure to feared social situations, within session and as homework; examination and modification of core beliefs; and relapse prevention and termination[86]	Reacting to and cognitively reappraising negative self-beliefs embedded in autobiographical social anxiety situations	During reactivity trials, CBT was associated with increased medial prefrontal cortex activation. During cognitive reappraisal trials, increased dorsolateral and dorsomedial prefrontal cortex, earlier temporal onset of dorsomedial prefrontal cortex activity, and greater dorsomedial prefrontal cortex-amygdala inverse functional connectivity
Goldin et al, 2014	Impact of cognitive-behavioral therapy for social anxiety disorder on the neural bases of emotional reactivity to and regulation of social evaluation	31 unmedicated adults (no other patient details given)	As per Goldin et al, 2013	Reacting to and reappraising images of social evaluation	For reactivity CBT resulted in increased brain responses in right superior frontal gyrus (SFG), inferior parietal lobule (IPL), and middle occipital gyrus (MOG) when reacting to social praise, and increases in right SFG and IPL and decreases in left posterior superior temporal gyrus (pSTG) when reacting to social criticism. For reappraisal CBT resulted in increased brain responses in right SFG and MOG, and decreases in left pSTG
OCD (n=5)					
Nakao et al, 2005	Brain activation of patients with obsessive-compulsive disorder during neuropsychological and symptom provocation tasks before and after symptom improvement: a functional magnetic resonance imaging study	10 medication free adults; 4 females, 6 males; mean age=32.4 years; no comorbidities	Behavior therapy, 12 weekly sessions lasting approximately 45 min. In the first session, the main problems were identified, and behavioral techniques were explained. Each patient then performed individually tailored home practice to expose themselves gradually to feared situations throughout the 12 sessions. Therapy was guided by experienced behavior therapists	Stroop and symptom provocation tasks	After symptom improvement, symptom provocation-related activation in the orbitofrontal, dorsolateral-prefrontal and anterior cingulate cortices decreased. Conversely, Stroop task-related activation in the parietal cortex and cerebellum increased.

Table I. Continued

decreased with symptom improvement after CBT. In another fMRI study examining the neural correlates of CBT for the most common OCD symptom dimension, namely contamination and washing obsessions, height-

Study (year)	Title of paper	Participant characteristics	CBT intervention	Brain imaging paradigm	Summary of findings (from publication abstracts)
Freyer et al, 2011	Frontostriatal activation in patients with obsessive-compulsive disorder before and after cognitive behavioral therapy	10 medication free adults; 3 females, 7 males; mean age=36.1 years; 1 patient had previous bulimia nervosa	Inpatient treatment duration varied from 8 to 12 weeks and was carried out by two experienced therapists specially trained in CBT with OCD patients, following a structured concept[87]	Probabilistic reversal learning (RL) task probing adaptive strategy switching capabilities	Decreased responsiveness of the orbitofrontal cortex and right putamen during strategy change before treatment in patients compared with healthy subjects. A group by time effect was found in the caudate nucleus, demonstrating increased activity for patients over the course of time. Patients with greater clinical improvement, reflected by greater reductions in Yale-Brown Obsessive Compulsive Scale (YBOCS) scores, showed more stable activation in the pallidum.
Huyser et al, 2011	Developmental aspects of error and high-conflict-related brain activity in pediatric obsessive-compulsive disorder: a fMRI study with a Flanker task before and after CBT	25 medication free pediatric patients; 16 females, 9 males; mean age=13.95 years; no comorbidities	16 sessions of manualized CBT consisting of exposure with response prevention and cognitive therapy suited to the needs of the patients[67]	Interference task, the arrow version of the Flanker paradigm	Increased activation of the ACC during error responses and in bilateral insular cortex during high-conflict tasks, which is age dependent and which is only partially affected by CBT
Olatunji et al, 2013	Predicting response to cognitive behavioral therapy in contamination-based obsessive-compulsive disorder from functional magnetic resonance imaging	12 adults; 6 female, 6 male; mean age=32.25 years; comorbidities included: social phobia; generalized anxiety disorder; major depressive episode; panic disorder without agoraphobia; specific phobia; body dysmorphic disorder; agoraphobia without panic; avoidant; obsessive–compulsive; depressive; dependent; borderline; paranoid; narcissistic; antisocial	12 weeks' CBT over 24 individual sessions. ERP strategies were used as a means of helping the patient discover the way in which neutralizing behavior acts to maintain their beliefs and the associated discomfort, and that stopping such behaviors is beneficial[90]	Symptom provocation with contamination-related images	Brain regions involved in emotional processing, such as the anterior temporal pole and amygdala, was most strongly associated with better treatment response. By contrast, activity in areas involved in emotion regulation, such as the dorsolateral prefrontal cortex, correlated negatively with treatment response mainly in the later stages within each block of exposure during symptom provocation.

Table I. Continued

ened activation of the amygdala and decreased dorso-lateral prefrontal cortex activation (associated with cognitive control) was indicative of significant reduction in anxiety symptoms after 12 weeks of CBT.[79] The authors concluded that in OCD successful recruitment of limbic structures during fear exposure may be beneficial for successful treatment outcome, whereas excessive top-down control via recruitment of the prefrontal cortex during CBT may hinder the effects of treatment.

Discussion

We have summarized contemporary models of anxiety and related disorders (eg, PTSD, PD, GAD, SAD, OCD) from the perspectives of animal studies and human magnetic resonance imaging (fMRI), in order to provide a foundation upon which to consider how CBT may alter the neurocircuitry of these conditions. We conclude that although each of the anxiety and related disorders is mediated by somewhat different neural circuitry, CBT may act in a similar way to increase prefrontal control of subcortical structures. In summary, anxiety disorders and PTSD are associated with exaggerated fear network activation to anxiety-provoking stimuli, involving limbic structures such as the amygdala, hippocampus, striatum, ACC, and insula.[1,3] Dysregulation in corticostriatal circuitry, on the other hand, is thought to underlie the neuropathology of obsessive-

compulsive and related disorders.[24] Such differences across circuitry may help explain symptom-specific traits for the various anxiety and related disorders, and may be considered targets for effective psychotherapy.[30] Discrete differences across these circuits may explain symptom-specific traits for the various anxiety and related disorders, and must be considered for effective psychotherapy. For example, fMRI studies of PTSD and PD report heightened activation of the fear network, particularly involving the amygdala and in response to anxiety-provoking stimuli,[35,44] while those with SAD show similar neural responses in the fear circuitry, but rather in relation to social stimuli.[50] Conversely, GAD has been linked to hypofunction in the PFC and ACC that is associated with emotion regulation,[47] and those with OCD show altered cortico-striatal-thalamic-cortical (CSTC) circuitry, and hyperactivation of both PFC and limbic networks.[19]

How CBT may affect neural function in the anxiety disorders

CBT is currently the most widely used and effective treatment for anxiety and related disorders,[60] although there are other effective treatments that will be mentioned below. An important outcome of CBT is improved emotional regulation.[61] Indeed, the data reviewed here suggest that neural circuitry underlying

| Study (year)	Title of paper	Participant characteristics	CBT intervention	Brain imaging paradigm	Summary of findings (from publication abstracts)
Morgiève et al, 2014	Dynamics of psychotherapy-related cerebral hemodynamic changes in obsessive compulsive disorder using a personalized exposure task in functional magnetic resonance imaging.	31 adults; 18 females 13 males; mean age 36.6 years;	3-month course of CBT 15 individual weekly 45-min sessions. Treatment plans were based on a reference manual[88] and were individually tailored to address patient specific symptoms, according to current standards[89]	Exposure task using neutral, generic and personalized obsession-inducing images.	Hemodynamic response to the task was located in the anterior cingulate and orbitofrontal cortices and was stronger during exposure to personalized obsession-inducing images. In addition, both the anxiety ratings and the haemodynamic response to the obsession-inducing images in the anterior cingulate and the left but not the right orbitofrontal clusters decreased with symptom improvement. Interestingly, hemodynamic activity continued to decrease after stabilization of clinical symptoms

Table I. Continued

emotion processing and regulation (prefrontal cortex and limbic system) appears most sensitive to change following psychotherapy of anxiety and related disorders.[91] That said, in terms of neural outcomes of CBT treatment for the various anxiety and related disorders, while there are broad similarities, there are also discrete differences. For example, CBT for PTSD is associated with greater left dorsal striatal and frontal network activation during inhibitory control, which may indicate that improvements to the inhibitory control neural network contribute to better treatment response.[63] CBT for PD correlates with increased activation between the PFC and regions of the fear network, such as the amygdala and hippocampus, which is related to improved cognitive appraisal of emotional responses.[64,65,92] In those with GAD, CBT appears to increase PFC activation, which may in turn be more effective at modulating pretreatment amygdala, hippocampal and insula activation, to enable better processing of positive and negative emotional stimuli.[49,68-70] For those with SAD, CBT appears to increase PFC and occipito-temporal activation that coincides with alterations in limbic circuitry and improvements in cognitive appraisal and emotionality.[71-74] Finally, in patients with OCD, reduced responses in limbic and other areas (including amygdala, striatum and ACC) appear to be most consistently observed following CBT, with some indication that PFC networks are strengthened.[54,76-79] However, it has also been suggested that excessive top-down control at the start of CBT may hinder the effects of treatment for OCD.[79] Some of these studies also suggest that pretreatment neural responses to disorder-specific stimuli may predict the effectiveness of CBT, and these findings are briefly discussed below. Regional brain functional differences associated with changes following CBT in anxiety disorders are shown in *Figure 2*.
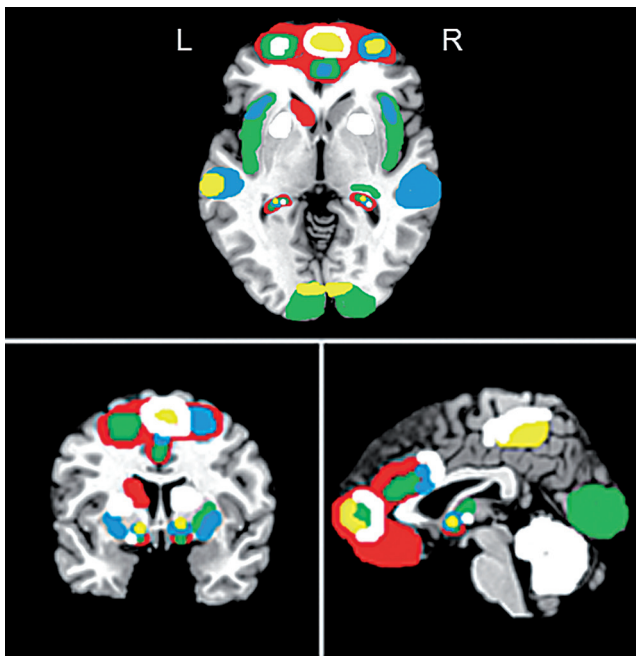
Figure 2. A schematic brain activation map demonstrating regional activation most altered by CBT in PTSD (red), PD (green), GAD (blue), SAD (yellow) and OCD (white). For demonstration purposes only and not accurate depiction of size of activation for each anxiety disorder. Colored regions represent areas of altered activation following a course of CBT. PTSD, post-traumatic stress disorder; PD, panic disorder; GAD, generalized anxiety disorder; SAD, social anxiety disorder; OCD, obsessive-compulsive disorder
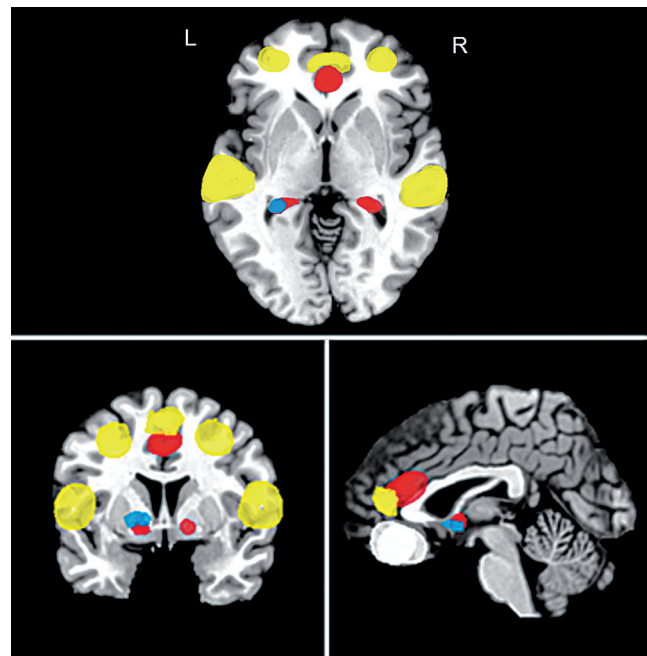
Figure 3. A schematic brain activation map demonstrating areas of pre-CBT treatment activation that predicts better outcome (eg, reduction of anxiety-related symptoms) in PTSD (red), PD (green), GAD (blue), SAD (yellow) and OCD (white). For demonstration purposes only and not accurate depiction of size of activation for each anxiety disorder. Colored regions represent areas of altered activation prior to CBT treatment that predicts improved outcome (eg, reduction of clinical symptoms). PTSD, post-traumatic stress disorder; PD, panic disorder; GAD, generalized anxiety disorder; SAD, social anxiety disorder; OCD, obsessive-compulsive disorder

Pre-CBT neural predictors of outcome

In a study of the effects of CBT on PTSD[80] only half the sample (n=7) were treatment responders (eg, at least 50% improvement on symptom severity scores). Poor treatment response was associated with pretreatment increases in bilateral amygdala and ventral ACC. The authors suggest that this could be indicative of significant dysregulation of the limbic system due to dysfunction of the PFC circuitry, which may adversely affect treatment success. Conversely, in patients with GAD, left amygdala hyperactivation prior to treatment predicted a reduction in clinical severity scores following CBT.[68] It was suggested that in those with GAD at least, a high level of emotional responsivity to disorder-salient stimuli at the start of treatment may help to drive the development of new cognitive strategies for the effective regulation of emotion after a course of CBT. In an fMRI study of SAD patients, increased pretreatment response to threatening faces in the superior and middle temporal gyrus, dorsal anterior cingulate cortex and dorsomedial prefrontal cortex predicted symptom reduction following CBT, and this may be indicative of an intact cognitive regulation PFC network that responds to treatment.[72] Neural activation during a reverse learning task in patients with OCD has also been associated with reduced OFC and striatal activation (caudate) prior to treatment.[76] Pre-CBT functional differences that may predict the effectiveness of treatment are illustrated in *Figure 3*.

Other treatments and the effects on neural processing

According to a recent meta-analysis of treatment studies for anxiety disorders,[60] a range of effective pharmacotherapies and psychotherapies exist. These include mindfulness therapies, which aim to focus cognitions on the breath, self and body sensations; relaxation, individual CBT, group CBT, psychodynamic therapy that brings nonconscious thoughts and feelings to the fore; therapies without face-to-face contact (eg, Internet therapies), eye movement desensitization reprocessing (EMDR) that uses eye movement to mimic sleep rhythms to reset emotional responses, and interpersonal therapy.

In terms of other psychotherapies, 8 weeks' mindfulness-based stress reduction in GAD patients appears to reduce hyperactivity in the amygdala, and increase VLPFC activation, which may suggest that mindfulness promotes regulation of emotion, or reduction of emo-

tional reactivity, as well as strengthening cognitive control of emotion in patients with GAD.[95] Mindfulness-based therapy in patients with SAD is associated with improved self-esteem, more positive self-appraisal, lowered anxiety and increased prefrontal cortex activation to emotional stimuli.[96] Internet-based CBT for patients with SAD is associated with a reduction in amygdala reactivity to emotional faces after treatment, as well as increased connectivity between the prefrontal cortex, ACC, and amygdala that corresponds to reductions in self-reported clinical symptoms and lack of relapse 1 year later.[97,98]

The relationship between genetic variants and neurocircuitry of CBT treatment

The effects of psychotherapy for anxiety and related disorders are likely to be influenced by the relationship between gene variants and neural circuitry pertaining to emotion regulation, however, more research needs to be conducted in this area. In one study, long alleles of the monoamine oxidase A (MAOA) gene in the uVN-TR promoter polymorphism region were linked to PD symptoms.[99] Those patients with the protective short alleles of the *MAOA* polymorphism had increased anterior cingulate cortex activation during fear conditioning in the presence of fearful stimuli at the beginning of CBT, and greater inferior parietal cortex activation after CBT. In another study of PD patients, inhibitory ACC-amygdala coupling during fear conditioning was characteristic of treatment response and was associated with presence of the L/L genotype of the serotonin transporter gene SLC6A4 *(5-HTTLPR)*.[64,100] Another study of PD patients showed inhibitory ACC-amygdala coupling during fear conditioning that had previously been shown to characterize treatment response in this sample was driven by CBT responders with the L/L genotype of the serotonin transporter gene.[101] Thus, there is growing evidence that genetic variation may be associated with specific alterations of neural responses during CBT of anxiety and related disorders.

Limitations and future directions

While there has been progress in knowledge of how psychotherapy for anxiety and related disorders impacts neural function, particularly in networks pertaining to cognitive regulation of emotion, there is still

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wide heterogeneity in fMRI studies, which prevents the drawing of firm conclusions. For example, fMRI studies typically utilize different paradigms, including fear conditioning, reverse learning, reappraisal, fear extinction, symptom provocation paradigms with anxiety-relevant stimuli and cognitive tasks (eg, response inhibition and reverse learning tasks such as Go/No Go and Flanker Tasks). On the one hand, such an approach is consistent with an emphasis on endophenotypes that are relevant across the anxiety and related disorders, and on the other hand there is also a need to clearly relate imaging work to the specific range of symptoms seen in the anxi-

ety and related disorders. Although the field has progressed, additional studies are clearly needed. While it is possible that brain-imaging technologies[102] will eventually generate single patient level predictions to guide clinical decision-making,[66] we are currently far from that point. In the interim, work on the neurocircuitry of psychotherapy has made an important contribution to the consolidation of both neurobiological models of anxiety and related disorders, as well as models of the mechanisms of treatment intervention. ❏

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Una revision sistemática de las bases neurales de la psicoterapia para la ansiedad y los trastornos relacionados

Los estudios de imaginología cerebral desde hace más de dos décadas han delineado los circuitos neurales de la ansiedad y los trastornos relacionados, particularmente las regiones involucradas en el procesamiento del miedo y en los síntomas obsesivo compulsivos. El circuito neural del procesamiento del miedo incluye la amígdala y las cortezas cingulada anterior e insular, mientras que el circuito tálamo-estriado-cortical juega un papel clave en el trastorno obsesivo-compulsivo. Más recientemente, los estudios de neuroimágenes han examinado cómo la psicoterapia para la ansiedad y los trastornos relacionados impacta en estos circuitos neurales. En este artículo se realiza una revision sistemática de los hallazgos de estos trabajos, los que comprenden 19 estudios de resonancia magnética functional que examinan las bases neurales de la terapia cognitivo-conductual (TCC) en 509 pacientes con ansiedad y trastornos relacionados. Se concluye que aunque la ansiedad y cada uno de los trastornos relacionados está mediado por circuitos neurales algo diferentes, la TCC puede actuar de manera similar para aumentar el control prefrontal de las estructuras subcorticales. Estos hallazgos son consistentes con el énfasis de la neurociencia cognitivo-afectiva en el potencial valor terapéutico del aumento de la regulación emocional en varias condiciones psiquiátricas.

Étude méthodique des bases neuronales de la psychothérapie pour l'anxiété et les troubles apparentés

Ces 20 dernières années, des études d'imagerie cérébrale ont défini les circuits neuronaux de l'anxiété et des troubles apparentés, en particulier les régions impliquées dans les processus de peur et les symptômes obsessionnels-compulsifs. L'amygdale, le cortex insulaire et le cortex cingulaire antérieur sont impliqués dans les circuits neuronaux des processus de peur, tandis que le circuit cortico-striato-thalamique joue un rôle dans les troubles obsessionnels-compulsifs. Plus récemment, des études de neuro-imagerie ont analysé comment la psychothérapie pour l'anxiété et les troubles apparentés influent sur ces circuits neuronaux. Nous menons ici une étude méthodique sur les résultats de ces travaux, qui a permis d'aboutir à 19 études d'imagerie fonctionnelle par résonance magnétique analysant les bases neuronales d'une thérapie cognitivo-comportementale (TCC) chez 509 patients atteints d'anxiété et de troubles apparentés. Bien que l'anxiété et les troubles apparentés soient induits par différents circuits neuronaux, nous concluons que la TCC peut agir de la même façon pour accroître le contrôle préfrontal des structures sous-corticales. Ces résultats sont cohérents avec l'accent mis dans les neurosciences cognitivo-affectives, sur la valeur thérapeutique potentielle de l'amélioration de la régulation émotionnelle dans diverses pathologies psychiatriques.

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